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MEMORANDUM

SUBJECT: *TERRAZOLE* - Report of the FQPA Safety Factor Committee.

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chair
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PC Code: 084701

The Health Effects Division (HED) FQPA Safety Factor Committee met on May 24, 1999 to evaluate the hazard and exposure data for terrazole and recommended that the FQPA Safety Factor (as required by the Food Quality Protection Act of August 3, 1996) be reduced to 3x in assessing the risk posed by this chemical.

I. HAZARD ASSESSMENT

1. Adequacy of Toxicity Database

There are data gaps for terrazole with regard to the standard Subdivision F Guideline requirements for a food-use chemical (40 CFR Part 158.340). A multi-generation reproduction study in rats and a chronic dog study are required. Pending submission and evaluation of these studies, additional studies (subchronic inhalation study, delayed neurotoxicity study in the hen, acute neurotoxicity study, subchronic neurotoxicity study and/or developmental neurotoxicity study) may be required (DRAFT Report of the HIARC; M. Centra to S. Knizner dated May 19, 1999).

2. Determination of Susceptibility

The HIARC concluded that the data provided no indication, either quantitatively or qualitatively, of increased susceptibility in rats or rabbits, to pre- and/or postnatal exposure to terrazole. In the prenatal developmental toxicity studies in rats and rabbits and the two-generation reproduction study in rats, any observed toxicity to the fetuses or offspring occurred at equivalent or higher doses than did toxicity to parental animals. And although the multi-generation reproduction study in rats was determined to be an unacceptable-guideline study and not adequate for regulatory purposes by the HIARC, it is noted that the observed offspring effects in this study occurred only at a treatment level which resulted in parental toxicity (DRAFT Report of the HIARC; M. Centra to S. Knizner dated May 19, 1999) .

II. EXPOSURE ASSESSMENT AND RISK CHARACTERIZATION

1. Dietary (Food) Exposure Considerations

Terrazole is currently registered for use on cotton (soil application; typical application rate is 0.20 lb.ai/A), turf (limited to golf course tees, greens and fairways; typical rate is 5.7 lb.ai/A), and seed treatment applications on barley, beans, corn, cotton, peanuts, peas, sorghum, soybeans, safflower, and wheat (application rates range from 0.005 to 0.25 oz.ai/A). There are no Codex MRLs for terrazole; therefore, no issues of compatibility with US tolerances exist.

The HED Metabolism Assessment Review Committee (5/11/99 meeting and 5/14/99 *ad hoc* meeting) has tentatively concluded that only the parent compound and its 3-carboxy metabolite should be included in both the tolerance expression and dietary exposure assessment.

No monitoring data are available for terrazole, however field trials indicate that no residues of terrazole or its 3-carboxy metabolite are expected on cottonseed, cotton gin byproducts, and cotton processed commodities as a result of in-furrow soil applications. No crop field trials were required or performed for terrazole as a seed treatment. Currently, seed treatment uses of terrazole are not being marketed.

At the time of this meeting, no dietary food exposure analyses using the Dietary Exposure Evaluation Model (DEEM) had been performed. Since no monitoring data or percent crop treated data are available for terrazole, it is expected that the analyses will include tolerance level residues and 100% CT for all commodities, resulting in an overestimate of dietary exposure to terrazole through food. However, if needed, the DEEM analyses could be refined to include anticipated residues calculated from field trial data and %CT data. Even if these refinements are made, the dietary food exposure estimates are still expected to be protective.

2. Dietary (Drinking Water) Exposure Considerations

The environmental fate data for terrazole are adequate to characterize drinking water exposure. These data indicate that the compound is mobile but not persistent and therefore, does not pose a concern for groundwater or surface water contamination.

Targeted monitoring data are not currently available. Tier I Estimated Environmental Concentrations (EECs) for terrazole were calculated using the GENEEC (surface water) and SCI GROW (groundwater) screening level models based on the highest application rate which was for a golf course scenario.

3. Residential Exposure Considerations

There are no registered residential uses, *per se*, for products containing terrazole. All registered products are for professional use only. However, golf course fairways, tees, and greens are treated with terrazole-containing products. Some turf products also include “landscape” and “interiorscape” uses. The potential exists for post-application exposure to anyone contacting areas that have been treated with these products. Turf studies have been submitted by the registrant and indicate a low transfer coefficient for treated turf residues, with a half-life of under six hours.

If a residential risk assessment is conducted, the *Draft Standard Operating Procedures for Residential Exposure Assessments* will be used to estimate the potential post-application exposure to infants and children.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendation

The Committee recommended that the **FQPA safety factor** for protection of infants and children (as required by FQPA) be **reduced to 3x**.

2. Rationale for Requiring the FQPA Safety Factor

The FQPA SFC concluded that a safety factor is required for terrazole since there is uncertainty due to the data gaps for the 2-generation reproductive study in rats.

The Committee recommended that the **FQPA safety factor** be **reduced** to 3x because:

- ▶ there is no quantitative or qualitative indication of increased susceptibility in the prenatal developmental toxicity studies in rats and rabbits;
- ▶ although the multi-generation reproduction study in rats was determined to be an unacceptable-guideline study and not adequate for regulatory purposes by the HIARC, it is noted that the observed offspring effects in this study occurred only at a treatment level which resulted in parental toxicity;
- ▶ adequate data are available or conservative modeling assumptions are used to assess the potential for dietary (food and drinking water) and residential exposure to infants and children.

Additionally, the Committee recommended that the weight-of-evidence for the FQPA safety factor recommendation be re-evaluated after all data requirements for terrazole have been satisfied.

3. Application of the Safety Factor - Population Subgroups

The FQPA safety factor is **applicable to all population subgroups** since there is uncertainty due to the data gap for the 2-generation reproduction study in rats which could identify potential reproductive effects to the parental animals or to the offspring following exposure to terrazole.

4. Application of the Safety Factor - Risk Assessment Scenarios

The FQPA safety factor for terrazole is **applicable to chronic dietary risk assessment and all residential risk assessments** since there is uncertainty for due to the data gap for the 2-generation reproduction study in rats which could identify potential reproductive effects to the parental animals or to the offspring following exposure to terrazole. The safety factor is **not applicable to acute dietary risk assessment** since no increased susceptibility was demonstrated following *in utero* exposure and the 2-generation reproductive study may not provide information on the potential for effects occurring after a single dose (exposure).